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Op-Ed submission to the Washington Post by Joshua Lederberg

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(Nobel-Laureate 1958 for research on genetics of microbes Dr. Lederberg was formerly a regular contributor to this editorial page.) \_\_\_\_\_

Smallpox research: Do we retain or burn the vicious bugs

Twenty years have passed since the last natural case of smallpox, until then one of the historic scourges of humankind. The eradication of human smallpox was a triumph of international public health cooperation and one of the great humanitarian accomplishments of our century. The major tool was universal vaccination, with special emphasis on the contacts of identified cases of the disease. By 1980, and on the advice from W.H.O. that the threat had vanished, most nations had suspended their vaccination programs. The only acknowledged remaining samples of the virus are those retained under high security in the U.S. city of Atlanta, and in the Siberian town of Koltsovo in Russia. Among public health workers, it has been a common understanding that these declared stocks would also be destroyed, by mutual agreement, once eradication of the natural disease had been certified and certain scientific studies of the virus had been completed.

In the last few years, many scientists have raised second thoughts about this step. Their

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voices reached President Clinton and on April 22 he announced a U.S. governmental decision to seek further delay of destruction of the virus, so as not to foreclose continued therapeutic research. This followed similar statements from the Russian Academy of Medical Sciences, as well as a scientific review by the U.S. Institute of Medicine -- an independent advisory body -- and a review within the U.S. government that led to an interdepartmental consensus recommendation to the President to delay destruction.

I strongly support President Clinton's declaration, though the arguments on both sides are complex, and reasonable people might disagree. Above all, we can hardly be certain that the smallpox virus is forever gone. It had to have evolved from its natural forebears in the first place, and close relatives like monkeypox are still fairly prevalent in the rainforests, occasionally reaching humans for outbreaks that until now have been self-limited. The same might have been said for the ancestors of the human immunodeficiency virus, which may have existed in other primates for thousands of years before we saw AIDS in humans.

It is understandable that many public health officers who have lent their careers to the eradication program would now favor the destruction of lab stocks -- "Burn the vicious bugs" would seem a natural culmination and a symbolic celebration of their humane and heroic efforts. But these stocks have rested quietly in the designated freezers for twenty years; destruction would be an irreversible step that would touch the interests of future generations for an indeterminate period.

If human smallpox reemerges, it will encounter a population utterly lacking immunity, as neither vaccination nor the natural disease will have hardened any part of the entire human herd. At present, we have no drugs to treat smallpox and the current vaccine is hazardous for

immunocompromised persons, such as those with HIV/AIDS. We need more scientific knowledge to be able to anticipate such events, and to design improved medications and vaccines to deal with a recurrent outbreak. This was the most important but highly promising value allocated to ongoing research by the IOM panel.

Even if smallpox per se is gone for good, laboratory studies on the virus continue to offer priceless lessons on how a virus achieves such exquisite adaptation to the human host, knowledge likely to be applicable to many other viral diseases. The live virus, as we decode its genome and understand the function of its parts, is a book of nature: burn it at peril of sustaining our ignorance.

The world's political and natural geography offers many more complications. The slogan of destroying the stocks may be mainly rhetoric, though it would be asymmetrically enforceable against the United States. There is no machinery of any kind to assure universal compliance with the doctrine. If it is to be adopted it should be associated with reliable means of verification and enforcement. Meanwhile there are credible allegations that smallpox has been an important part of the Soviet biological weapons program.

Even if the declared stocks at Koltsovo were destroyed, most observers have little confidence that this would touch the clandestine Russian military biological weapons programs. These have not been clarified since the admissions by Gorbachev and by Yeltsin on ongoing work in violation of the 1975 BW disarmament convention. Furthermore, we have no idea what may have been retained, maliciously or inadvertently, in the laboratories of a hundred other countries from the time that smallpox was a common disease. These would be the most likely sources of supply for possible bioterrorists. And there are Nature's own freezers in the

graveyards located in the Arctic tundras.

We cannot let the matter rest with a reprieve. Retention of the stocks, in Russia and the U.S. is only justified if this can be certified as part of a safe and efficient program meeting global health interests. We should therefore promptly initiate formal negotiations towards setting up an international regime to regulate the registration of extant stocks, oversight of their safety and security, and broad participation in decisions about the research that we might need to call upon in future. And all countries in the world should receive the benefits of this important research, should they ever be needed. We have a shared responsibility for the welfare of the entire globe. These arrangements should be formalized, so that illicit or unregistered retention of virus stocks be the subject of effective legal sanctions, at a national and an international level.

None of these conditions now attach to the simplistic "Burn the Vicious Bugs" doctrine which will be reviewed on May 17th at WHO, and which the World Health Assembly has the opportunity to amend. It is now time for deliberate reconsideration that will enable a well-regulated option for research that will safeguard us all.